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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

| EXAMINER | |
|---|---|
| CARTER, KENDRA D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/801,856 | KRAMER ET AL. | |
| | Examiner | Art Unit | |
| | KENDRA D. CARTER | 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5 and 11-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The Examiner acknowledges the applicant's remarks and arguments of June 16, 2008 made to the office action filed March 14, 2008. Claims 1-5 and 11-16 are pending. Claims 1 and 2 are amended and claims 15 and 16 are new. Claims 6-10 are canceled.

In light of the amendments, the claim objection of claim 2 is withdrawn.

Applicant's arguments were found not persuasive, thus the following rejections are upheld: 1) the 35 U.S.C. 112, second paragraph rejection of claim 1; and 2) the 35 USC 102(b) rejection of claims 1, 3, 4 and 13 as being anticipated by Chen et al.; and 3) the 35 USC 103(a) rejection of claims 2, 5, 11, 12 and 14 as being unpatentable over Chen et al. in view of Moskowitz.

Due to the amendment to the claims, the modified and new rejections are made below. Applicant's arguments are addressed below.

### *Claim Rejections - 35 USC § 102*

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Chen et al. (US 6,383,471 B1).

Chen et al. teach a pharmaceutical composition comprising a hydrophobic therapeutic agent such as zolpidem and pharmaceutically acceptable salts (see claim 11; addresses claims 1 and 2), and a carrier comprising an ionizing agent (i.e. pH buffer; see applicant's specification page 7, lines 9-10; addresses claim 3), surfactant (i.e. penetration agent; see column 23, line 46; column 27, line 17; applicant's specification page 7, line 3) and triglyceride (i.e. nasal carrier; see claim 1; addresses claim 1; see applicant's specification page 6, line 14). The composition can be formulated for transmucosal administration in the form of an ointment, gel, or sprayable solution (i.e. nasal administration via a pressurized or non-pressurized spray; see column 35, lines 10-14 and 20; addresses claims 1 and 13). The carrier is able to solubilize the ionizable hydrophobic therapeutic agent and maintain the therapeutic agent in solubilized form for improved delivery to the absorption site (see column 4, lines 37-40). The solubilization of the therapeutic agent depends upon the therapeutic agent being ionized with the ionizing agent (see column 12, lines 51-52). Salts of the drug may be used advantageously for the sake of salt exchange with the acid or base ionizing agent, leading to better salt selection (see column 10, lines 42-26). The amount of hydrophobic therapeutic agent to be used depends upon the dosage amount to be delivered. One skilled in the art can determine the appropriate dosage amount, depending upon the specific hydrophobic therapeutic agent to be delivered, the nature

of the condition treat, the relative efficacy of the therapeutic agent, and other factors commonly considered (see column 10, lines 55-61). The carrier includes on or more pharmaceutically acceptable solubilizers to enhance the solubility of the drug such as water (see column 31, lines 40-44 and column 32, line 6; addresses claim 2). The amount of solubilizer is limited to a bioacceptable amounts (see column 32, lines 52-54; addresses claim 2). For compositions in the form of an aqueous dispersion, the pre-concentrate form is prepared, then the appropriate amount of purified water is added and the solution gently mixed (see column 35, lines 34-37).

In regards to the composition being under pressure or not, but in an aerosol or spray, the Examiner views the Chen et al. teaches this limitation. Particularly, Chen et al. teach a transmucosal administration (i.e. nasal) in the form of a sprayable solution (see column 35, lines 10-14 and 20). Thus, the broad teaching reads on both pressurized or non-pressurized.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**1) Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6,383,471 B1) as applied to claims 1, 3, 4 and 13, in view of Merkus (US 6,007,834).**

The teachings of Chen et al. are as applied to claims 1, 3, 4 and 13 above.

Chen et al. does not specifically teach a composition under pressure in a pressurized container or in a non-pressurized container.

Merkus teaches that the insomnia composition comprising melatonin (see column 4, lines 31-47), administered via a nasal spray (see column 2, lines 46-53). The spray can be in a pump spray device with a metering pump, or alternatively comprise a pressurized spray device (see column 3, lines 51-67).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and in which the composition is under pressure in a pressurized container or in a non-pressurized container because of the following teachings: 1) Chen et al. teach a transmucosal administration (i.e. nasal) in the form of a sprayable solution (see column 35, lines 10-14 and 20); 2) zolpidem is an insomnia drug; and 3) Merkus teaches a nasal spray insomnia (see column 4, lines 31-47; see column 2, lines 46-53) composition, in which the spray can be in a pump spray device with a metering pump, or alternatively

comprise a pressurized spray device (see column 3, lines 51-67). Thus, one skilled in the art would be able to formulate the nasal composition of the insomnia drug zolidem as taught by Chen et al. in a pressurized or non-pressurized spray device with the expectation of successful treatment.

**2) Claims 2, 5, 11, 12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6,383,471 B1) as applied to claims 1, 3, 4 and 13, in view of Moskowitz (US 5,767,177).**

The teachings of Chen et al. are as applied to claims 1, 3, 4 and 13 above.

Chen et al. does not specifically teach a solution of a 2:1 zolpidem/tartrate salt in sterile purified water (claim 2), or the amounts of zolpidem disclosed in claims 5, 11 and 12. Chen et al. also does not specifically teach wherein the composition is buffered to a ph of 3 to 10.

Moskowitz teaches a method of treating migraine headaches with compounds that directly or indirectly activate GABA receptors (see abstract and claim 1) such as zolpidem in 100 μg/kg (see claim 7 and column 13, line 23) or between 0.01 mg/kg to 2000 mg/kg per day (see column 10, line 11).

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and a 2:1

zolpidem/tartrate salt in sterile purified water as disclosed in claim 2 because of the following teachings of Chen et al.: 1) the pharmaceutical composition comprises a hydrophobic therapeutic agent such as zolpidem and pharmaceutically acceptable salts (see claim 11); 2) salts of the drug may be used advantageously for the sake of salt exchange with the acid or base ionizing agent, leading to better salt selection (see column 10, lines 42-26); 3) the carrier includes on or more pharmaceutically acceptable solubilizers to enhance the solubility of the drug such as water (see column 31, lines 40-44 and column 32, line 6); 4) for compositions in the form of an aqueous dispersion, the pre-concentrate form is prepared, then the appropriate amount of purified water is added and the solution gently mixed (see column 35, lines 34-37); and 5) the amount of solubilizer is limited to a bioacceptable amounts (see column 32, lines 52-54). Thus one skilled in the art would be able to formulate the salt formation of the drug and the ratio because it is advantageous to the composition in regards to solubization and what is bioacceptable to the patient.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and the amounts of zolpidem disclosed in claims 5, 11 and 12 because of the following teachings: 1) Chen et al. teach the amount of the hydrophobic therapeutic agent to be used depends upon the dosage amount to be delivered and that one skilled in the art can determine the appropriate dosage amount, depending upon the specific hydrophobic therapeutic agent to be delivered, the nature of the condition treat, the relative efficacy of the therapeutic

agent, and other factors commonly considered (see column 10, lines 55-61); 2) Moskowitz teaches a method of treating migraine headaches with zolpidem in 100 μg/kg (see claim 7 and column 13, line 23) or between 0.01 mg/kg to 2000 mg/kg per day (see column 10, line 11); and 3) it is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of the result effective variable in a known process is ordinarily within the skill of the art." See, e.g., In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Paterson* Appeal No. 02-1189 (Fed. Cir. January 8, 2003). Thus, one skilled in the art would be able to determine the appropriate amount of zolpidem to comprise in the composition based on the information provided above.

To one of ordinary skill in the art at the time of the invention would have found it obvious and motivated to combine the composition of Chen et al. and wherein the composition is buffered to a ph of 3 to 10 (claim 14) because Chen et al. teach that the composition comprises an ionizing agent (i.e. pH buffer; see applicant's specification page 7, lines 9-10), in which the solubilization of the therapeutic agent depends upon the therapeutic agent being ionized with the ionizing agent (see column 12, lines 51-52). Thus, upon ionization of zolpidem, the composition will obviously be between the pH of

3 to 10 in order to be solubilized. Particularly, the ionization of zolpidem will result in a basic solution in order to be solubilized, which can fall within the pH range of 8-10.

***Response to Arguments***

Applicant's arguments have been fully considered but they are not persuasive.

> The Applicant argues that Chen et al. does not disclose or suggest a nasal administration that is in liquid form and is in a pressurized or non-pressurized container. Moskowitz does not remedy the deficiency of Chen et al.

The Examiner disagrees that Chen et al. does not teach a liquid sprayable nasal administration pharmaceutical that can be in a pressurized or non-pressurized container. Particularly, Chen et al. teach a transmucosal administration (i.e. nasal) of hydrophobic therapeutic agent such as zolpidem (see claim 11) in the form of a sprayable solution (see column 35, lines 10-14 and 20). Thus, the broad teaching of sprayable solution reads on both pressurized or non-pressurized.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KENDRA D. CARTER whose telephone number is (571)272-9034. The examiner can normally be reached on 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/K. D. C./
Examiner, Art Unit 1617

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617